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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/664,432	09/19/2003	Charles E. Hart	00-12D1	5728

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EXAMINER	
JIANG, DONG	
ART UNIT	**PAPER NUMBER**
1646	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/12/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/664,432	HART ET AL.	
	Examiner	Art Unit	
	Dong Jiang	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-9,11-13 and 22-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-9,11-13 and 22-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/12/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED OFFICE ACTION

Applicant's election of Group I invention, and the species election of IGF-1, filed on 21 July 2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Applicant's amendment filed on 21 July 2006 is acknowledged and entered. Following the amendment, claims 1, 10 and 14-21 are canceled, and claims 2, 3, 5-9, 11, 22 and 26 are amended.

Currently, claims 2-9, 11-13 and 22-26 are pending and under consideration.

Formal Matters:

Information Disclosure Statement

Applicant's IDS submitted on 12/12/2005 is acknowledged and has been considered. A signed copy is attached hereto.

Priority determination

This application claims benefit of U.S. applications 09/823,033 filed on 3/29/01, and 09/457,066 file on 12/7/99, and U.S. provisional applications 60/193,723 filed on 3/31/00, 60/165,255 filed 11/12/99, 60/161,653 filed on 10/21/99, 60/142,576 filed on 7/6/99, and 60/111,173 filed on 12/7/98. However, for the following reasons, the Examiner finds that the instant claims are not fully supported in the manner required by 35 U.S.C. 112 by the prior applications.

With the exception of U.S. application 09/823,033 filed on 3/29/01, none of the other prior applications discloses the use of zvegf3 of SEQ ID NO:2 in promoting growth of bone, ligament, or cartilage. In fact, application 09/457,066 filed on 12/7/99 (09/823,033 is a CIP of 09/457,066) suggests the opposite, i.e. it indicates that Zvegf3 *antagonists* are of interest in the treatment of inflammatory disorders, such as rheumatoid arthritis (page 83, lines 5-7), which is a disorder

characterized by cartilage destruction. Therefore, the present claims are not entitled to the benefit of the filing date of those prior applications. Priority is granted to the filing date of the application 09/823,033, 3/29/01.

Specification

The specification is objected to because the status of U.S. Application 09/823,033, which has been issued as U.S. Patent No. 6,663,870, has not been updated yet.

Claims

Claims 6 and 24 are objected to for the following informalities, appropriate correction is required for each item:

In line 2 of the claims, "a bone-targetting agent" should be "a bone-targeting agent".

Rejections under 35 U.S.C. 112:

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 13 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The claim is directed to a method for promoting growth of bone, ligament, or cartilage by administering a composition of a dimeric protein comprising polypeptide chains of residues X-345 of SEQ ID NO:2, wherein X is an integer from 15 to 20. However, the specification provides no guidance or support for such use, and prior art search reveals contrary evidence. For

example, Eriksson et al. (US7,034,200) teaches a human platelet derived growth factor, PDGF-C, which amino acid sequence of SEQ ID NO:1 is 100% to the present SEQ ID NO:2. Further, Eriksson teaches that PDGF-C requires proteolytic removal of the N-terminal CUB domain for receptor binding and activation of the receptor, which is 110 amino acid long (column 4, lines 42-51). Therefore, the present Zvegf3 molecule (SEQ ID NO:2) comprising polypeptide chains of residues X(15 to 20)-345 of SEQ ID NO:2 would not be functionally active, and thus, it would not be suitable for the recited use. As such, the claimed method is not enabled.

Rejections Over Prior Art:

The following rejections under 35 U.S.C. § 102 and 103 are made in view of the determination that the effective filing date for the instantly claimed invention is 3/29/01, which is the actual filing date of the prior application 09/823,033, and is relied upon in the instant application for an earlier filing date under 35 U.S.C. 120.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 2-5, 8, 9, 11, 12, 22, 23, 25 and 26 are rejected under 35 U.S.C. 102(e) as being anticipated by Eriksson et al., US2002/0164687 A1, and as evidenced by Camacho et al., US6,934,576 B2.

Eriksson discloses a human platelet derived growth factor, PDGF-C, which amino acid sequence of SEQ ID NO:3 is 100% identical to the present SEQ ID NO:2. Additionally, Eriksson teaches that the full length PDGF-C is likely to be a latent growth factor that needs to be activated by proteolytic processing to release an active PDGF/VEGF homology domain, and that a putative proteolytic site is found in residues 231-234 in the full length protein (page 8, [0076]). Further, Eriksson teaches the truncated PDGF-CC homodimers (cPDGF-CC) (page 14, line 1 of the left column), and demonstrates that truncated PDGF-CC, but not full length PDGF-CC, effectively induced PDGF-Rα tyrosine phosphorylation, indicating that truncated PDGF-CC

is a potent PDGF-Rα agonist (page 14, the last four lines of the 1st paragraph of the left column). Furthermore, Eriksson teaches that PDGF-C has the ability to stimulate and/or enhance proliferation or differentiation and/or growth and/or motility of cells expressing a PDGF-C receptor including, among others, connective tissue cells (page 4, [0031]), which include the recited bone, ligament and cartilage (the present claim 11, for example), as evidenced by Camacho (column 4, lines 16-18). Furthermore, Eriksson teaches a pharmaceutical composition of PDGF-C useful for therapeutic applications, which comprises PDGF-C and a suitable pharmaceutical carrier or diluent such as an ester of a long chain fatty acid (abstract, page 4, [0031], and page 7, [0065] and [0066]); and a method of stimulation of connective tissue development in a mammal in need of such treatment by administering an effective dose of PDGF-C (page 6, [0056]. As such, the reference anticipates claim 11 and the dependent claims 2, 9, 12, 22, 23 and 26. Note, although the reference does not explicitly mention stimulating proliferation of osteoblasts or chondrocytes (as claim 22, for example), it would be the inherent property once the PDGF-C composition is administered for the purpose of promoting (stimulating) growth of connective tissue cells such as bone, ligament and cartilage. Furthermore, Eriksson teaches that suitable routes of administration include, systemically: oral, subcutaneous, intramuscular or intravenous injection (systemically), or locally: topical application, implants etc. (page 7, [0064]). Thus, Therefore, the reference also anticipates claims 3-5. Furthermore, Eriksson teaches that optionally the PDGF-C may be administered together with PDGF-A or PDGF-B. Thus, the reference anticipates claims 8 and 25.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Eriksson et al., US2002/0164687 A1, and as evidenced by Camacho et al., US6,934,576 B2, as applied to claims 2-5, 8, 9, 11, 12, 22, 23, 25 and 26 above.

The teachings of Eriksson are reviewed above. Additionally, Eriksson teaches that the doses and rote of administration will also depend upon the nature of the patient and condition to be treated, and will be at the discretion of the attending physician or veterinarian (page 7, [0064]. The reference does not explicitly teach local administration of PDGF-C at a joint.

However, it would have been obvious to the person of ordinary skill in the art at the time the invention was made to treat a subject with conditions such as arthritis (cartilage destruction) by locally injecting the PDGF-C because Eriksson teaches that PDGF-C has the ability to stimulate proliferation, differentiation and/or growth of connective tissue cells (including cartilage), and that PDGF-C can be used locally, depending upon the nature of the condition to be treated, and the discretion of the attending physician, and because arthritis is characterized by cartilage destruction of joints. The person of ordinary skill in the art would have been motivated to do so for disease treatment such as arthritis, and reasonably would have expected success because Eriksson teaches that PDGF-C has the ability to stimulate proliferation, differentiation and/or growth of connective tissue cells.

Claims 6 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Eriksson et al., US2002/0164687 A1, and as evidenced by Camacho et al., US6,934,576 B2, as applied to claims 2-5, 8, 9, 11, 12, 22, 23, 25 and 26 above, and further in view of Bentz et al., EP 0 512 844 A1.

The teachings of Eriksson are reviewed above. The reference does not explicitly teach covalently linking the PDGF-C to a bone-targeting agent.

Bentz teaches a composition comprising a bone growth factor and a bone-targeting agent, and a method of use thereof for augmenting bone formation or treating bone defects or bone loss, and for bone repair in a subject (column 4, lines 29-44, and column 7, lines 50-52). Further, Bentz teaches that targeted delivery of bone growth factors may reduce harmful or undesirable effects of those molecules, allow the use of lower doses because relatively higher doses can be delivered to the site of interest, and prolong the effect, and that a targeting molecule that influences bone metabolism may result in an additive or synergistic effect (column 4, lines 18-25).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to link the PDGF-C taught by Eriksson to a bone-targeting agent such as those taught by Bentz for bone repair or treating bone defects or bone loss because targeted delivery may reduce undesirable effects, allow the use of lower doses and prolong the effect, and may result in an additive or synergistic effect, as indicated by Bentz. The person of ordinary skill in the art would have been motivated to do so for bone disease treatment, and for the advantages of targeted delivery as taught by Bentz, and reasonably would have expected success because Eriksson teaches that PDGF-C has the ability to stimulate proliferation, differentiation and/or growth of connective tissue cells, and Bentz has successfully demonstrated the conjugations comprising a bone growth factor and a bone-targeting agent.

Conclusion:

No claim is allowed.

Advisory Information:

Any inquiry concerning this communication should be directed to Dong Jiang whose telephone number is 571-272-0872. The examiner can normally be reached on Monday - Friday from 9:30 AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Dong Jiang

Dong Jiang, Ph.D.
Patent Examiner
AU1646
10/8/06